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The Role of Vitamin D in Adults Requiring Nutrition Therapy

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Abstract

The major and most well known function of vitamin D is to maintain calcium and phosphorus homeostasis and promote bone mineralization. However, recent evidence suggests that vitamin D may also be important for a variety of non-skeletal outcomes. The review synthesizes the available evidence for the role of vitamin D in skeletal health as well as its novel roles in medical conditions such as muscle function, falls, immunity, glucose homeostasis and cardiovascular diseases. It reviews methods for assessing vitamin D status and it suggests strategies to restore vitamin D status in patients requiring enteral or parenteral nutrition who are at particularly high risk of hypovitaminosis D. Screening for hypovitaminosis D with plasma total 25(OH)D should be a routine part of the care of the patient requiring enteral or parenteral nutrition. Restoration of optimal vitamin D status with high dose supplemental vitamin D is required in most cases, while exposure to sunlight or an ultraviolet B radiation-emitting device is most effective in patients with severe malabsorption or those requiring chronic parenteral therapy. Given the emerging role of vitamin D for a variety of acute and chronic conditions, the optimal vitamin D status in acutely ill patients as well as in patients requiring long-term nutrition therapy warrants further investigation.

Keywords

Vitamin D; nutrition support; nutrition therapy

Introduction

The major and most well known function of vitamin D is to maintain calcium and phosphorus homeostasis and promote bone mineralization. However, recent advances have revealed that vitamin D status may also be important for a variety of non-skeletal outcomes. The purpose of the review was (1) to synthesize the available evidence on the role of vitamin D in medical conditions seen in the inpatient populations including those requiring nutrition therapy, such as muscle function and falls, fractures, compromised immunity, glucose intolerance and cardiovascular disease and (2) to review methods for assessing vitamin D status and (3) to suggest strategies to restore vitamin D status in patients requiring enteral or parenteral nutrition.

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Precis: Hypovitaminosis D is prevalent and it is associated with increased risk for a variety of acute and chronic medical conditions. Assessment of vitamin D status and reversal of vitamin D deficiency has become increasingly important in patient care including patients requiring nutrition therapy.

Literature Search and Data Synthesis

We searched MEDLINE for English-language literature through December 2008 for: (1) observational studies on the association between vitamin D status and outcomes, (2) intervention studies of the effect of vitamin D supplementation (3) systematic reviews or comprehensive narrative reviews on the role of vitamin D, in inpatient populations with special focus among those requiring nutrition therapy. Search terms included diabetes, hyperglycemia, glucose, metabolic syndrome, cardiovascular disease, metabolic bone disease, fracture, falls, immune system, infection, autoimmunity, inpatient, hospital, nutrition therapy, enteral nutrition, parenteral nutrition, vitamin D, and related terms. Additional publications were identified from citations from the recovered articles, review articles and personal reference lists and we selected those with judged relevant.

Review of vitamin D homeostasis

The sources of vitamin D include cutaneous synthesis (in the form of cholecalciferol [D₃]) and intake (from diet and/or supplements in the form of D₃ or, less frequently, ergocalciferol [D₂]). Upon exposure to solar ultraviolet B radiation (UVB), 7-dehydrocholesterol in the skin is converted to previtamin D₃, which is immediately converted to vitamin D₃ in a heat-dependent process. Humans have evolved to derive the majority of their vitamin D requirement from cutaneous synthesis, so vitamin D is found in high amounts in only a few foods (hereafter “D” represents D₂ or D₃) (Table 1). The most important dietary sources of vitamin D are commonly consumed foods that are fortified with vitamin D, such as milk and breakfast cereals, or supplements containing vitamin D (Table 1). Whether endogenously synthesized or ingested, vitamin D is bound to the vitamin D-binding protein and is transported to the liver where it is converted to 25-hydroxyvitamin D (25[OH]D), its major circulating form. This form of vitamin D is biologically inactive. Under the influence of parathyroid hormone (PTH) and vitamin D status, 25(OH)D is converted primarily in the kidney to its active circulating metabolite, 1,25-hydroxyvitamin D (1,25[OH]₂D), by the enzyme 25(OH)D-1α-hydroxylase (CYP27B1). The primary action of 1,25(OH)₂D is through the vitamin D receptor to enhance intestinal calcium absorption and promote the maturation of osteoclasts, thereby maintaining calcium and phosphorus homeostasis and bone health. However, it has been increasingly recognized that vitamin D has pleiotropic effects in a variety of extra-skeletal tissues suggesting an important role in health and prevention of disease as discussed below.

Assessment of vitamin D status

Because of its long half-life, plasma 25(OH)D concentration is considered the best measure for assessing vitamin D status.^{1, 2} Low 25(OH)D concentration has been correlated with classic conditions of vitamin D deficiency such as hypocalcemia, secondary hyperparathyroidism, rickets and osteomalacia, while improvements in circulating 25(OH)D have been correlated with recovery from these conditions.^{3, 4} The most widely used method to quantify 25(OH)D is by radioimmunoassay. Automated direct detection methods, such as chemiluminescence, HPLC and liquid chromatography-mass spectroscopy (LC-MS) assays have become increasingly common, especially in large medical centers. The latter two methods quantify and report 25(OH)D₂ and 25(OH)D₃ separately. However, it is not clear whether this separation is useful in clinical practice, as nearly all patients tested will have no detectable circulating 25(OH)D₂ unless they have been treated with ergocalciferol (D₂). Since there is evidence that separate reporting may confuse interpretation by physicians,⁵ it is recommended that in routine clinical practice the total 25(OH)D be reported and evaluated.⁶

Vitamin D binding protein decreases with injury or trauma, and reduced concentrations appear to reflect severity of illness and predict eventual morbidity or mortality.^{7, 8} However, after an initial decrease early after an acute illness, synthesis of vitamin D binding protein increases.⁹

Reductions in this protein may in part reflect its role as an actin scavenger, with increased consumption associated with injury. Whether changes in vitamin D binding protein that accompanies acute illness affect measured 25(OH)D concentrations is unclear. Free vitamin D concentration appears to be well maintained in patients with reduced vitamin D binding protein secondary to chronic malabsorption or liver disease, indicating that the total 25(OH)D level is accurate as an indicator of vitamin D status among those with severe illness.² In general, 1,25(OH)₂D should not be measured to assess vitamin D status as those with hypovitaminosis D may have normal 1,25(OH)₂D concentration as a result of secondary hyperparathyroidism. Additionally, the elimination half-life of 1,25(OH)₂D is very short.

Measurement of 25(OH)D is sometimes accompanied by measurement of serum calcium and PTH concentrations. In healthy populations and in many chronic conditions, PTH elevations reflect secondary hyperparathyroidism in response to hypovitaminosis D. However, provision of parenteral nutrition (PN) may complicate the relationship between measured vitamin D, calcium and PTH. In PN patients receiving nocturnal infusions that contained calcium, the evening diurnal rise in PTH was blunted. When calcium was removed from PN, the normal diurnal rise was no longer suppressed.¹⁰

Another factor further complicating interpretation of 25(OH)D among those requiring nutrition therapy may be the accelerated bone resorption seen in immobilized patients. In a study of chronically disabled stroke patients, concentrations of both 25(OH)D and 1,25(OH)₂D were low, and there was no correlation between 25(OH)D and PTH. Increases in serum ionized calcium were associated with reduced concentrations of 1,25(OH)₂D but were not associated with concentrations of 25(OH)D. Further degree of 25(OH)D deficiency did not predict 1,25(OH)₂D concentration.¹¹ Therefore, treatment of 25(OH)D deficiency in those with accelerated bone resorption due to immobilization may not necessarily lead to expected increases in the active 1,25(OH)₂D.

In general, biochemical markers that are routinely measured in acutely or chronically ill patients are likely to be of little value in suggesting the presence of hypovitaminosis D. Serum measurements of calcium and phosphorus are influenced by many factors. In hospitalized ill patients, hypoalbuminemia has been a predictor of hypovitaminosis D in some but not all studies.¹²⁻¹⁵ Hypophosphatemia with initiation of enteral feeding is not uncommon in hospitalized patients, especially in those at risk for refeeding syndrome. Hypovitaminosis D may impair phosphate absorption from food, enteral nutrition products, and from supplements. Hypophosphatemia seen during enteral feeding should stimulate consideration of assessment of vitamin D status.

Vitamin D status in the population

As described below, there is controversy as to the optimal 25(OH)D level; however, most experts agree that a level below 20 ng/ml (50 nmol/L) is considered “deficiency” while a level below 30 ng/ml (75 nmol/L) is considered “insufficiency”.^{16, 17} Data from NHANES III show that vitamin D insufficiency may affect the majority of the non-institutionalized population in the US, even in the southern latitudes during the winter.¹⁸⁻²¹ Additional studies have shown a prevalence of hypovitaminosis D ranging from 36-100% in a variety of populations worldwide, from healthy young adults to hospitalized elderly individuals.^{12, 20, 22-29} As expected, vitamin D deficiency is much more common in high-risk populations, such as homebound elderly and hospitalized persons who are sun-deprived and have suboptimal nutrition,^{12, 24, 30} overweight/obese individuals, as well as among those with darker skin such as Non-Hispanic blacks and Hispanics.^{19, 31, 32}

Risk factors for hypovitaminosis D

There are multiple risk factors for hypovitaminosis D, as outlined in Table 2. Approximately 80% of the variation in vitamin D status among individuals can be explained by differences in cutaneous synthesis as a function of UVB exposure and skin color.³³ As 25(OH)D concentration is inversely related to body weight and body fat,^{34, 35} excess body weight is another important predictor of vitamin D status in the setting of increasing prevalence of obesity. After gastric bypass surgery for obesity, vitamin D status does not necessarily normalize and these patients remain at risk for hypovitaminosis D, secondary hyperparathyroidism, and metabolic bone disease.^{36, 37} The risk for vitamin D deficiency may be related, in part, to the degree of systemic inflammation.³⁸

Hospitalized patients, especially those with prolonged hospitalizations or in long-term care facilities, including those who require short-term or long-term enteral or parenteral nutrition, are at particularly high risk for vitamin D deficiency as they exhibit many of the major risk factors, including lack of exposure to UVB light, suboptimal vitamin D intake, advanced age and diseases or medication influencing vitamin D metabolism.

Similar to healthy individuals, lack of sun exposure increases risk for hypovitaminosis D in hospitalized patients,^{12, 39, 40} as is prolonged hospitalization. Additionally, although dietary intake of vitamin D is less important than UVB exposure in healthy individuals, the association between poor intake of vitamin D and hypovitaminosis D is heightened with inpatients.^{12, 13, 40} Chronic illness prior to hospitalization may contribute to both poor intake and reduced sun exposure.

Vitamin D absorption is influenced by a number of gastrointestinal diseases. Patients with Crohn's disease^{41, 42} and celiac disease⁴¹ are at risk for hypovitaminosis D as well as long-term metabolic bone disease. Vitamin D status is also impaired by cholestatic liver disease, such as primary biliary cirrhosis,⁴³ and pancreatic insufficiency with its associated malabsorption (e.g. cystic fibrosis^{44, 45}). Non-cholestatic cirrhosis may also be associated with impaired vitamin D status as loss of hepatocytes may result in reduced synthesis of 25(OH)D. However, not all studies have confirmed reductions in 25(OH)D in these patients,^{14, 46} probably reflecting less advanced disease with preserved 25-hydroxylase function. Chronic kidney disease is commonly associated with hypovitaminosis D, at least in part due to reduced activity of 25(OH)D-1 α -hydroxylase. Nephrotic syndrome may lead to increased urinary losses of vitamin D and vitamin D binding protein.

Vitamin D, health outcomes, and implications for hospitalized patients

Emerging data demonstrate that the health implications of impaired vitamin D status are widespread and of potentially great clinical significance, as reviewed below.

The discovery that nearly all tissues in the body express the vitamin D receptor and that several tissues also express the 25(OH)D-1 α -hydroxylase, which allows for local production of 1,25(OH)₂D with a paracrine effect, has provided new insights in the role of vitamin D in several medical conditions. Hypovitaminosis D has been associated with increased all-cause and cardiovascular mortality,⁴⁷ while a recent meta-analysis of randomized trials showed that intake of ordinary doses of vitamin D supplements was associated with a modest decrease in total mortality.⁴⁸ However, it is important to note that because the risk factors for vitamin D deficiency are also risk factors for many acute and chronic medical conditions, vitamin D status is an excellent marker of overall health; therefore, the observational studies linking hypovitaminosis D with suboptimal health may not reflect a true association because of potential residual or unmeasured confounding.

Musculoskeletal function

Musculoskeletal disability and falls are a common occurrence in the hospital and long-term care facilities.⁴⁹⁻⁵¹ Several observational studies have reported an association between vitamin D insufficiency and poor lower extremity muscle performance, gait imbalance and increased risk of falls.⁵²⁻⁵⁴ Randomized trials have also shown improvements in muscle performance after vitamin D supplementation.⁵⁵⁻⁵⁹ A meta-analysis, which assessed the effectiveness of vitamin D in preventing falls, concluded that vitamin D supplementation reduces the risk of falls among ambulatory or institutionalized older individuals by more than 20 percent.⁵⁹ Recent trials have also supported a beneficial role of supplemental vitamin D on falls;^{60, 61} however, other trials found no effect.⁶²⁻⁶⁴ Two of the trials with neutral results were conducted in the outpatient setting where the baseline incidence of falls is low. Vitamin D is thought to improve muscle function by having a direct effect on myocytes, which express vitamin D receptors, to increase the cross-sectional area of type IIA muscle fibers.⁶⁵

The evidence on the effect of vitamin D on bone health and fractures varies between studies. An evidence-based review combining data from 13 trials found a non-significant reduction in fractures but with significant heterogeneity between studies.⁶⁶ The effect appears to be maximal when a high dose vitamin D (700-800 international units [17.5–20 µg]/day) is given in older persons living in institutionalized settings.

Vitamin D deficiency is also associated with osteomalacia, which in adults presents with non-specific complaints of malaise, fatigue and body aches and can be debilitating to the patient and frustrating for the clinician to diagnose. Restoring vitamin D status can reverse symptoms of osteomalacia.⁶⁷

Metabolic Bone Disease

A complicating factor in patients receiving parenteral nutrition (PN) is the occurrence of metabolic bone disease. This has been reported in the majority of patients receiving long-term home PN.⁶⁸ Several factors have been implicated in the cause of PN-associated metabolic bone disease, including calcium deficiency, aluminum toxicity and amino-acid solutions. The role of vitamin D in the pathogenesis of PN-associated metabolic bone disease has been controversial. It has been suggested that, in the absence of a requirement for enteral calcium absorption, the amount of vitamin D found in the multivitamin PN solution may be toxic to the bone. It has been hypothesized that in those patients with suppressed PTH, provision of parenteral vitamin D contributes to metabolic bone disease.⁶⁸ In two studies, withdrawal of vitamin D from PN was associated with improvement in the clinical and biochemical indices of bone mineralization.^{69, 70} In these studies, vitamin D status, as assessed by 25(OH)D level, was suboptimal by current criteria. No reports in the last decade have confirmed these findings. In a recent study, bone mineral loss in patients on long-term PN was similar as in age and gender-matched controls,⁷¹ suggesting that underlying disease itself may be responsible for metabolic bone disease and PN is less likely to promote metabolic bone disease.

Immune system, infections and autoimmunity

Infections are prevalent in hospitals and long-term facilities. Inpatients are exposed to a large number of pathogens and the risk of acquiring an infection rises when immunity is compromised. Several lines of evidence suggest an important role of vitamin D as a regulator of the immune system.⁷² In observational studies, vitamin D deficiency has been found to be associated with development of infections, including influenza and tuberculosis.^{73, 74} Infants with rickets are at increased risk for respiratory infection.^{75, 76} There is also limited data from randomized trials to suggest that vitamin D supplementation may prevent infections.^{77, 78} A direct role of vitamin D in immunity is suggested by the expression of the vitamin D receptor by the majority of immune cells, including antigen-presenting cells like macrophages and

dendritic cells, as well as activated CD4 and CD8 T-lymphocytes.⁷⁹ Moreover, macrophages express 25(OH)D 1- α -hydroxylase (CYP27B1), which allows local synthesis of the active form of vitamin D.^{72, 80} These findings suggest a fundamental role of vitamin D on the innate immune system and a potentially important role in preventing infections among susceptible individuals, including those who required long-term enteral/parenteral nutrition therapy. Finally, there have been several studies reporting an association between hypovitaminosis D and a variety of autoimmune diseases, including type 1 diabetes, multiple sclerosis, inflammatory bowel disease and rheumatoid arthritis.⁸¹⁻⁸⁴ Vitamin D is thought to act as an immunosuppressive agent by suppression of type 1 T-helper cytokine profile, which favors suppressor T cells (type 2 T-helper).⁸⁵

Glucose Homeostasis and Cardiovascular Disease

Diabetes and cardiovascular disease (hereafter termed 'cardiometabolic disease') are major causes of morbidity and mortality in the industrialized world. On the basis of evidence from animal and human studies, vitamin D has now emerged as a potential modifier of cardiometabolic risk.⁸⁶ Vitamin D insufficiency has long been suspected to be a risk factor for type 1 diabetes.⁸⁷ More recently, there is accumulating evidence to suggest that altered vitamin D homeostasis may also play a role in the development of type 2 diabetes and cardiovascular disease. Observational studies have reported a consistent association between hypovitaminosis D and incident type 2 diabetes⁸⁸ or cardiovascular disease.^{47, 89, 90} Evidence from randomized trials on cardiometabolic disease is limited. A *post-hoc* analysis of a trial designed for bone-related outcomes showed a beneficial effect of combined vitamin D₃ (700 international units [17.5 μ g] / day) and calcium (500 mg/day) supplementation on preventing the rise in glycemia that occurs over time among those with glucose intolerance at baseline.⁹¹ However, a *post-hoc* analysis from the large Women's Health Initiative trial showed no effect of combined vitamin D₃ (400 international units [10 μ g] /day) and calcium (1000 mg/day) supplementation on incident cardiovascular disease⁹² or self-reported diabetes.⁹³ In the Women's Health Initiative, the neutral results can be explained by the low dose of supplemental vitamin D₃, which is considered insufficient for both skeletal and non-skeletal outcomes. Congestive heart failure has also been associated with increased risk for hypovitaminosis D.^{94, 95} Patients with congestive heart failure supplemented with vitamin D show reduced concentrations of inflammatory cytokines, although it remains unclear if this could translate to improved myocardial function or delayed disease progress.⁹⁶ Several ongoing trials are expected to offer further insights into the role of vitamin D on cardiometabolic disease. The potential effects of vitamin D on the cardiometabolic system are thought to be mediated by a variety of mechanisms, including improving pancreatic beta-cell function, enhancing insulin action in insulin-sensitive tissues, ameliorating systemic inflammation, regulating smooth muscle function and inhibiting the renin-angiotensin system.⁹¹

Vitamin D Supplementation

The Food and Nutrition Board of the Institute of Medicine set the adequate intake (AI) of vitamin D at 200-600 international units (5-15 μ g) / day based on age.³ In the Nurses Health Study, a large prospective observational cohort, we found that only 3% of female nurses reported the recommended vitamin D intake for their age. However, there is growing consensus that vitamin D intakes above these levels are associated with better health outcomes. The optimal plasma 25(OH)D concentration is hotly debated but for a variety of skeletal and non-skeletal outcomes, most experts agree that a level above 30 ng/ml (75 nmol/l) is required to improve outcomes.⁹⁷ To achieve this desired level of 25(OH)D, an intake of at least 1,000 international units [25 μ g] /day of vitamin D is needed.^{97, 98} Levels of 25OHD much higher than 30 ng/ml (75 nmol/l) need to be individualized because risk of nephrolithiasis increases and hypercalcemia may be unmasked in patients with granulomatous disease or asymptomatic

primary hyperparathyroidism. Oral formulations of vitamin D are available either as cholecalciferol (D₃) or ergocalciferol (D₂) (Table 1). In general, supplementation with vitamin D₃ is preferred over D₂ because the latter may be less bioactive and may have lower affinity for the vitamin D receptor,⁹⁹ although data are conflicting.¹⁰⁰ However, which type of vitamin D is preferred may not be very relevant in clinical practice because nearly all over-the-counter dietary supplements and foods fortified with vitamin D contain vitamin D₃ while the only high-dose vitamin D available as a prescription formulation, is vitamin D₂ (Table 1). Vitamin D₂ is the only vitamin D form available as a pharmaceutical preparation because it predated the Food and Drug Administration' and thus, was grandfathered as a pharmaceutical drug. Vitamin D₃ has not been approved as a pharmaceutical agent in the United States.¹⁰⁰ Effective supplementation can be achieved either on a daily, weekly or monthly basis.¹⁰¹ The amount of vitamin D in commonly used enteral nutrition formulations (Table 3) is consistent with the official recommendations by the Food and Nutrition Board.³ However, ill patients will likely need much higher intakes of vitamin D because of aging, lack of sun exposure and other factors such as malabsorptive syndromes or renal disease.

Our recommendation is to first confirm hypovitaminosis D (plasma 25[OH]D < 30 ng/ml (75 nmol/l)), and then administer 50,000 international units (1,250 µg) of vitamin D₂ weekly for 12 weeks followed by 1,000 international units [25 µg] vitamin D₃ daily. Alternatively, as high-dose vitamin D formulations become available, the initial high ("loading") dose of vitamin D₂ may be substituted for an equivalent dose of vitamin D₃. This regimen raises 25 (OH)D concentration above 30 ng/ml (75 nmol/l) in most patients. However, in patients with severe malabsorption syndromes, doses as high as 50,000 international units (1,250 µg) per day may be needed to adequately raise 25(OH)D levels. Frequent monitoring for hypercalcemia (preferably with measurement of ionized calcium) is recommended, especially when daily high-dose regimens are prescribed. To avoid hypercalciuria, a 24-hour urine collection for measurement of calcium and creatinine may be considered; results of 24-hour urine excretion of calcium in patients maintained by oral or enteral nutrition can be interpreted by use of current normal ranges, but interpretation in patients on PN may be influenced by a number of factors that render interpretation more difficult.

Given the lack of requirement for calcium absorption, patients who are exclusively on PN do not require vitamin D for calcium absorption; however, given the direct effects of vitamin D on parathyroid cells and osteocytes, and its pleiotropic effects on tissues not involved in calcium homeostasis, maintaining optimal vitamin D levels is important in this population as well. The difficulty with patients requiring PN is determining the optimal level of vitamin D. In patients requiring long-term PN, frequent measurements of 25(OH)D, 1,25(OH)₂D, parathyroid hormone and calcium and maintenance of these markers as close to normal as possible is important. Vitamin D supplementation in patients who require PN is also challenging because of the lack of a high-dose parenteral formulation of vitamin D. Currently, patients on PN receive a daily multivitamin injection, which contains 200-400 international units (5-10 µg) of vitamin D₂ or D₃, depending on the product. There is an intramuscular form of high-dose vitamin D (not available in the US) with decreased bioavailability that can cause significant discomfort; therefore it is not recommended. An alternative and quite effective method to improve vitamin D status in individuals with malabsorption syndromes and those on chronic PN, is exposure to sunlight or UVB radiation from a tanning bed or other UVB emitting device.¹⁰² On rare occasions, such as with hypercalcemia or hypervitaminosis D, elimination of vitamin D from PN may be desired; however, vitamin D is included as a standard component of parenteral multivitamins and there is no known multivitamin preparation for infusion that does not contain vitamin D.

Conclusions

Vitamin D deficiency or insufficiency is very common, especially among hospitalized patients requiring long-term enteral or parenteral nutrition, and it is associated with increased risk for a variety of acute and chronic medical conditions including musculoskeletal disease, fractures, infection and cardiometabolic disease. Screening for vitamin D deficiency with plasma 25(OH)D should be a routine part of the care of the patient requiring enteral or parenteral nutrition therapy. Restoration of optimal vitamin D status with high dose supplemental vitamin D is required in most cases, while exposure to sunlight or UVB-emitting device could be most effective in patients with severe malabsorption or those requiring chronic PN therapy. There are several unresolved questions that need further investigation, including the role of vitamin D in the pathogenesis of PN-associated metabolic bone disease, the optimal 25(OH)D level in patients requiring nutrition therapy especially among those exclusively on chronic PN therapy, and the best modality for restoring vitamin D status. Given the emerging roles for vitamin D in inflammation and glucose homeostasis, the influence of vitamin D status and vitamin D provision on outcomes in hospitalized patients deserves further attention.

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Table 1

Dietary and supplemental sources of vitamin D*

	Amount	
	International Units	Micrograms
Natural foods		
Cod liver oil	400 - 1000 / teaspoon	10 - 25
Oily fish (3.5 oz) Salmon,		
Fresh, wild	600 - 1000	15 - 25
Fresh, farmed	100 - 250	2.5 - 6.75
Sardines, canned	300	7.5
Mackerel, canned	250	6.25
Tuna, canned	230	5.75
Egg yolk	20	0.5
Fortified Foods	100 / serving	2.5
Milk		
Orange Juice		
Most cereals		
Some yogurt		
Supplemental		
Cholecalciferol (D ₃)		
Multivitamin	400	10
Vitamin D only pill	400, 800, 1000, 2000, 5000, 10000	10, 20, 25, 50, 125, 250
Vitamin D only liquid	1000, 4000 per serving	25, 100
Ergocalciferol (D ₂)		
Prescription pill (generic)	50,000 per capsule	1,250 per capsule
Prescription liquid (Drisdol)	8,000 per ml	200 per ml
Intramuscular **	300,000 - 600,000 per injection	7,500 – 15,000

* Vitamin D₃ unless specified

** Intramuscular vitamin D is not available in the U.S. as a standard formulation.

Table 2**Major risk factors for vitamin D deficiency**

Risk Factor	Example
Reduced skin synthesis	
Limited UVB exposure	Latitude >37°, season, time of day, weather Protective clothing, sunscreen Physical inactivity, homebound Repeated UVB exposure/tanning Air pollution
Skin pigmentation	Dark skin
Decreased intake	Unhealthy diet / limited supplement intake Intestinal malabsorption syndromes Parenteral nutrition
Decreased bioavailability	Sequestration of vitamin D (not conclusively shown to occur in humans)
Increased catabolism	Glucocorticoids, antiepileptic drugs (carbamazepine, phenytoin)
Aging	All of the above (physical inactivity, etc.) Other (decreased cutaneous synthesis, lactose intolerance)
Decreased synthesis of 25(OH)D	Liver failure
Reduced synthesis of 1,25(OH) ₂ D	Chronic kidney disease

Table 3

Vitamin D content in selected total enteral nutrition preparations

Selected Enteral Nutrition Preparations	Vitamin D₃ (international units / liter)
2CalHN® (Abbott Laboratories, USA)	425
Promote® (Abbott Laboratories, USA)	400
Promote® with Fiber (Abbott Laboratories, USA)	400
Peptamen AF™ (Nestle Nutrition, USA)	328
Jevity® 1 Cal (Abbott Laboratories, USA)	305
Osmolite® 1 Cal (Abbott Laboratories, USA)	305
Glucerna® 1.2 Cal (Abbott Laboratories, USA)	285
Peptamen® (Nestle Nutrition, USA)	272
Nepro® with Carb Steady™ (Abbott Laboratories, USA)	85
Renalcal® (Nestle Nutrition, USA)	0

40 international units = 1 µg